

## ABSTRACT

Proteins in the IKK and JNK signaling pathways, such as NF $\kappa$ B, are involved in  
5 the regulation of inflammatory diseases. Through phosphorylation and polyubiquitination, I $\kappa$ B proteins which sequester NF $\kappa$ B in the cytoplasm, are degraded by the ubiquitin-proteasome pathway releasing NF $\kappa$ B to the nucleus where it is activated. The present invention provides methods utilizing the composition of proteins in the IKK,  
10 JNK and ubiquitin-proteasome pathways such as, TRAF6 or TRAF2 (E3-ubiquitin protein ligase), TRIKA1/Uev1A/Ubc13 complex (E2-ubiquitin conjugating enzyme), and TRIKA2/TAK1 (protein kinase), in screening for candidate modulators involved in activation of the IKK and JNK pathways. The application further provides methods of utilizing the candidate modulators as drug therapeutics against inflammatory and immune diseases.